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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/478,222	01/05/2000	DAVID S. GARVEY	102258.346	1404

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EXAMINER

CELSA, BENNETT M

ART UNIT	PAPER NUMBER
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1627

DATE MAILED: 01/22/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

file
copy

Office Action Summary

Application No.

09/478,222

Applicant(s)

Garvey et al.

Examiner

Bennett Celsa

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE three MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Sep 26, 2001
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 35-69 is/are pending in the application.
- 4a) Of the above, claim(s) 35-60 and 66-69 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 61-65 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- *See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) ☐ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 0, 14, 1!
- 18) ☐ Interview Summary (PTO-413) Paper No(s) _____
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other:

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DETAILED ACTION

Response to Amendment

Applicant's amendment dated 9/26/01 in paper no. 8 is hereby acknowledged.

Status of the Claims

Claims 35-69 are currently pending.

Claims 61-65 are under consideration.

Claims 35-60 and 66-69 are withdrawn from consideration as being directed to a non-elected invention.

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Election/Restriction

2. This application contains claims 35-60 and 66-69 drawn to a nonelected invention. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Withdrawn Objection(s) and/or Rejection(s)

3. Applicants' submission of a terminal disclaimer has obviated the obviousness-type double patenting rejection of claims 61-65 over the pending claims (e.g. claims 8-11) of copending Application No. 09/354,424 in view of Stamler et al. US Pat. No. 5,380,758 (1/10/95) and Gioco et al., U.S. Pat. No. 5,565,466.

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4. Applicant's argument, declaration and general incorporation by reference were sufficient to overcome the new matter rejection of claims 61-65 under 35 U.S.C. 112, first paragraph.

Outstanding Objection(s) and/or Rejection(s)

5. Claims 61-65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stamler et al. US Pat. No. 5,380,758 (1/10/95) and Gioco et al., U.S. Pat. No. 5,565,466 (10/96: filed 8/93).

Stamler et al teach the that S-nitrosothiols achieve both smooth muscle and and blood vessel relaxation (e.g. *vasodilation*) and are useful to treat male sexual dysfunction (e.g. impotency) by administration (E.g. topical) of S-nitrosothiol compounds, including the use of S-nitrosylated amino acids and peptides (e.g. S-nitrosoglutathione) which are clearly within the scope of the presently claimed invention (e.g. see Stamler et al. at Abstract; col. 1, lines 20-37; bottom of col. 2- top of col. 4; col. 4, lines 45-55); col. 11; patent claims 1-3, 14-16, 20-23).

Although teaching the use of S-nitrosothiols to treat impotence in males, the Stamler reference differs from the presently claimed invention in failing to teach the use of the same agent (e.g. S-nitrosothiols) to treat impotence in females.

The Gioco et al. Patent discloses that male and female impotency would be expected to be treated similarly (e.g. by use of vasodilating agents) since the erectile response: is common to both males and females (e.g see col. 1, 20-30), shares common characteristics (E.g. result of blood engorgement of erectile tissues in response to sexual stimulation) and is treated similarly

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e.g. with the administration (e.g. topical) of *vasodilating* agents (e.g. see col. 1, lines 10-20; col. 3, lines 45-65; col. 4-7).

Thus, the Gioco patent reference provides one of ordinary skill in the art with motivation to utilize S-nitrosothiols to treat female impotency in the same manner as in the treatment of males as disclosed in Stamler, since Gioco teaches that the erectile response in males and females is similar and amenable to similar treatments including the utilization of vasodilating agents which would encompass S-nitrothiols.

Accordingly, it would have been obvious to one of ordinary skill at the time of applicant's invention to use (e.g. topical administration) S-nitrosothiol compounds (e.g. S-nitrosyl-glutathione) to treat female impotence in the manner disclosed in the Stamler reference in light of the Gioco reference teaching.

Discussion

Applicant's arguments directed to the above obviousness rejection were considered but deemed nonpersuasive for the following reasons.

Applicant argues that "the PTO has already established that the use of compounds to treat male sexual dysfunctions does not render prima facie obvious the use of the same compounds to treat female sexual dysfunctions" citing patents (e.g. Patents 5, 708,031; 5,718,917; 5,877,216; 5,945,117; 5,770,606; 5,565,464; and 5,565,464 and purported prosecutions histories involving such patents.

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Applicant's argument is irrelevant to the case at hand since every application stands or falls on its own merits. In any event, is also noted that applicant's argument can easily be interpreted as supporting the above obviousness rejection, since compounds useful in males have been found similarly useful in female (and vice versa) in the treatment of sexual dysfunction.

Applicant next argues that there is no motivation to combine the Stamler and Gioco reference teachings.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the Stamler and Gioco references clearly address the same problems (e.g. sexual dysfunctions) and are clearly within the knowledge generally available to one of ordinary skill in the art who is addressing the problem of sexual dysfunctions. Additionally, both references address the same overall solution to the problem e.g. the use of vasodilating agents. Accordingly, one of ordinary skill in the art would have ample motivation to combine the Stamler and Gioco reference teachings.

Applicant further argues that neither the Stamler nor the Gioco reference taken separately teach the use of S-nitrosothiols to treat female sexual dysfunctions.

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In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In response to the Gioco reference teaching applicant cites "obvious differences" and "one common aspect" language found in Gioco and further argues that female sexual response is more complex than male response (e.g. both physically and mentally) and that one commonality does not provide any reason for one to believe that the treatments would be the same. In this respect applicant further cites references e.g. Berman et al. (1999); Levin (1991); Halvorsen et al. (1992) which outline some of the differences in the female response which are not present in the male response (e.g. clitoral erection, vaginal blood flow etc.). Applicant still further cites Goodnow (1997) for the premise that female treatments for female sexual dysfunctions have been inappropriately based upon studies in males.

Initially, it is noted that the Examiner questions the relevancy on an obviousness inquiry of citing references which were unavailable to one of ordinary skill in the art *at the time of applicant's invention* (e.g. see Goodnow or Berman articles).

In any event, applicant's argument mischaracterizes the above obviousness rejection which is not based on "one common aspect" as asserted by applicant. In this regard, the above obviousness rejection clearly asserts that the male and female erectile responses (e.g. impotency) are recognized by the prior art as being similar (e.g. share common characteristics and tissue) and

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are thus similarly treated e.g. the use of vasoactive agents (e.g. vasodilating agents). Accordingly, the use of a specific vasodilator (e.g. S-nitrosothiols) in males for treating impotency would be *reasonably expected* to be useful to treat impotency in females. In this respect, the test of obviousness is “reasonable expectation” and not absolute certainty.

Neither applicant’s argument mischaracterizing the above rejection, nor citing references that discuss known differences in male and female sexual responses or articles that indicate, in some instances, treatment of female sexual dysfunctions have been inappropriately based upon studies in males overcome the reasonable expectation that vasodilating agents (e.g. S-nitrosothiols) known to treat male impotency would be reasonably expected to be similarly useful in females given the shared characteristics of male/female impotency and the established use of vasodilators in women to treat impotency.

Accordingly, for the reasons recited above, the obviousness rejection is hereby retained.

Double Patenting

6. Claims 61-65 are provisionally rejected under the judicially created doctrine of provisional obviousness-type double patenting as being unpatentable over the pending claims (e.g. claims 20-66, especially claims 20, 31-33) of copending Application No. 09/280,540 in view of Stamler et al. US Pat. No. 5,380,758 (1/10/95) and Gioco et al., U.S. Pat. No. 5,565,466 (as discussed above and incorporated by reference).

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Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of application '540 teach a method of treating female sexual dysfunction using S-nitrosothiols. To the extent that the '540 claims fail to teach treatment of a species of female sexual dysfunction (E.g. female impotence) as presently claimed, treating female impotence using S-nitrosothiols would have been obvious in view of Stamler and Gioco which teach that S-nitrosothiols treat male impotence (e.g. Stamler) to which female impotence would be treated similarly in view of Gioco's teaching that female and male impotence is amenable to the same treatment (e.g. especially using vasodilating agents such as S-nitrosothiols)..

Discussion

Applicant's arguments directed to the above obviousness-type double patenting as being unpatentable over the pending claims (e.g. claims 20-66, *especially claims 20, 31-33*) of copending Application No. 09/280,540 in view of Stamler et al. and Gioco were considered but deemed nonpersuasive for the following reasons.

Applicant argues that claims 20-66 are directed to compositions which *combine* alpha adrenergic receptor antagonists and nitric oxide donor compounds (including S-nitrosothiols) and their method of use for treating sexual dysfunctions which differ from the present claims which address the use of S-nitrosothiols alone to treat female impotence which is asserted to be different and patentably distinct.

However, applicant's argument is misguided in several respects.

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First, it ignores the '540 application claims teaching of the use of S-nitrosothiols alone or combined with alpha adrenergic receptor antagonists (which are encompassed by the present claims use of "comprising" language in the composition) to treat female sexual dysfunctions.

To the extent that applicant is arguing that the claims fail to teach the specific female sexual dysfunction (e.g female impotence), applicant is reminded that one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicant's argument regarding patentable distinctness is not relevant regarding what the '540 application claims teach to one of ordinary skill in the art which is at issue in the above double patenting rejection.

The Examiner's arguments above in rebuttal of applicant's arguments regarding the inability of the combined teaching of the Stamler and Gioco reference to arrive at the presently claimed invention in the above obviousness rejection, is hereby incorporated by reference in its entirety.

Accordingly, the above obviousness-double patenting rejection is hereby retained.

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7. Claims 61-65 are provisionally rejected under the judicially created doctrine of provisional obviousness-type double patenting as being unpatentable over the pending claims (e.g. claims 35-56, especially claims 41 and 44-46) of copending Application No. 09/306,809 in view of Stamler et al. US Pat. No. 5,380,758 (1/10/95) and Gioco et al., U.S. Pat. No. 5,565,466 (as discussed above and incorporated by reference).

Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of application '809 teach a method of treating female sexual dysfunction using S-nitrosothiols. To the extent that the '809 claims fail to teach treatment of a species of female sexual dysfunction (E.g. female impotence) as presently claimed, treating female impotence using S-nitrosothiols would have been obvious in view of Stamler and Gioco which teach that S-nitrosothiols treat male impotence (e.g. Stamler) to which female impotence would be treated similarly in view of Gioco's teaching that female and male impotence is amenable to the same treatment (e.g. especially using vasodilating agents such as S-nitrosothiols)..

Discussion

Applicant's arguments directed to the above obviousness-type double patenting as being unpatentable over claims 35-56 of copending Application No. 09/306,809 in view of Stamler et al. and Gioco were considered but deemed nonpersuasive for the following reasons.

Applicant argues that claims 35-56 are directed to compositions which *combine* alpha adrenergic receptor antagonists of formula III alone or in combination with nitric oxide donor compounds (including S-nitrosothiols) and their method of use for treating sexual dysfunctions

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which differ from the present claims which address the use of S-nitrosothiols alone to treat female impotence which is asserted to be different and patentably distinct.

However, applicant's argument is misguided in several respects.

First, it ignores the '809 application claims teaching of the use of S-nitrosothiols alone or combined with alpha adrenergic receptor antagonists (which are encompassed by the present claims use of "comprising" language in the composition) to treat female sexual dysfunctions.

To the extent that applicant is arguing that the claims fail to teach the specific female sexual dysfunction (e.g female impotence), applicant is reminded that one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicant's argument regarding patentable distinctness is not relevant regarding what the '809 application claims teach to one of ordinary skill in the art which is at issue in the above double patenting rejection.

The Examiner's arguments above in rebuttal of applicant's arguments regarding the inability of the combined teaching of the Stamler and Gioco reference to arrive at the presently claimed invention in the above obviousness rejection, is hereby incorporated by reference in its entirety.

Accordingly, the above obviousness-double patenting rejection is hereby retained.

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8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

General information regarding further correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Celsa whose telephone number is (703) 305-7556.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jyothsna Venkat (art unit 1627), can be reached at (703)308-0570.

Any inquiry of a general nature, or relating to the status of this application, should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Bennett Celsa (art unit 1627)

January 16, 2002

BENNETT CELSA
PRIMARY EXAMINER

